REMARKS

This application is believed to be in condition for allowance at the time of the next Official Action.

Status of the Claims

Claims 1-5, 7-11, 15, 17-25 remain in this application.

Claims 2-5, 7-11, 15, 19-25 have been withdrawn.

Claim Rejections-35 USC §112

Claims 1, 17 and 18 were rejected under 35 U.S.C. §112, second paragraph, for being indefinite. This rejection is respectfully traversed for the reasons below.

The position of the Official Action was that the meaning of "hydrophilic" and "lipophilic" are unclear in the context of the invention, e.g., in light of the disclosed main constituents for the matrix and the Examples.

Paragraph 32 of the originally filed specification states:

> "The term "hydrophilic nature" or "essentially hydrophilic nature" is intended to mean a matrix that is solely hydrophilic in nature, or else lipophilic and hydrophilic in nature, the hydrophilic nature being, in this case, predominant with respect to the lipophilic nature in the medium of interest. Similarly, the term "lipophilic nature" or "essentially lipophilic nature" is intended to mean a vector that is solely lipophilic in nature, or else lipophilic and hydrophilic in nature, the lipophilic nature being, in this case, predominant with respect to the hydrophilic nature in the medium of interest. In the remainder of the present disclosure, it will be understood that, firstly, the terms "matrix that is (essentially) hydrophilic in nature" and "hydrophilic matrix" are equivalent and, secondly, that the terms "vector that is (essentially) lipophilic in nature" and "lipophilic vector" are equivalent."

The main constituent of the hydrophilic matrix of the vector is in general selected from polylactates, poly(lactate-co-glycolate)s (subsequently referred to as PLGAs), polymers or copolymers based on hyaluronic acid, on chitosan, on starch, on dextran and on the like, and also copolymers thereof and mixtures thereof. It may, for example, be envisioned that the main constituent of the matrix is a PLGA-hyaluronic acid, PLGA-chitosan, PLGA-starch or else PLGA-dextran mixture, or other mixtures.

While the matrix may include polymers or copolymers based on materials having a lipophilic nature, such as chitosan, paragraph 32 of the specification explains that the matrix is "essentially hydrophilic". That is, the nature of the matrix is hydrophilic or the predominant nature is hydrophilic. Indeed, in Example 2, it is noted that the matrix is a mixture of chitosan, and the hydrophilic sodium hyaluronate.

Thus, the meaning of an "essentially hydrophilic" matrix and the selection of components to form such matrix are believed to clear in light of the specification.

Therefore, the claims are definite, and withdrawal of the rejection is respectfully requested.

Claim Rejections-35 USC §103

Claims 1 and 17-18 were rejected under 35 U.S.C. § 103(a) as being obvious over KUMAR Journal of Pharmacy and

Pharmaceutical Sciences 2000 3: 234-258 ("KUMAR") in view of KELLER US 6,726,924 ("KELLER") and BAKER et al. US 6,534,018 ("BAKER"). This rejection is respectfully traversed for the reasons below.

The claimed invention is directed to a vector for the oral administration of at least one pharmacologically active substance.

The aim of the invention is to provide such a vector that is able to go through the gastrointestinal tract and to pass across the intestinal wall. The major advantage of the claimed vector is that the vector prevents the active substance from degrading and denaturing during passage across the intestinal wall. Also see, e.g., the present specification at page 6, lines 8-16.

Consequently, it is necessary that the vector is of a size that allows the physical passage of the vector across the intestinal membrane.

This necessary size of the vector is, thus, less than 300 nm, e.g., 200-300 nm as presently recited in claim 1.

It is also essential that the vector remains unchanged before crossing the intestinal membrane. The vector is degraded only after crossing the intestinal membrane, and, thus, allowing the active substance to be released in the blood or in the interstitial fluid, i.e., as recited in claim 1.

Claim 1, the independent claim, describes a vector that comprises an essentially hydrophilic matrix having an outer surface modified with one or more chemical species, wherein the chemical species detach from the matrix upon contact with microvilli present in the intestine.

KUMAR discloses microspheres comprising a cross-linked chitosan matrix containing 5-FU as the pharmacologically active substance, and the outer surfaces of the microspheres are modified with a DPPC lipid multilayer. These crosslinked chitosan microspheres coated with the lipid multilayer are used for delivering 5-FU (page 247, Figure 10). KUMAR describes the lipid coating layers on the microspheres as being effective barriers to 5-FU release in physiological saline at 37°C, and the phase transition temperature of the coating layers is 41.4°C (page 248, left column, 1st and 2nd paragraph).

However, KUMAR fails to disclose that the DPPC lipid multilayer detaches from the chitosan matrix.

Indeed, there is no suggestion that upon contact with microvilli during passage through the intestinal lumen, the DPPC lipid multilayer would detach from the chitosan matrix such that the matrix becomes essentially hydrophilic in nature. On the contrary, as mentioned above, this multilayer is effective to prevent the release of 5-FU at up to 41.4°C.

KELLER and BAKER fail to remedy the deficiencies of KUMAR for reference purposes, as neither document suggests the modification by chemical species of the outer surface of a hydrophilic matrix containing an active substance. KELLER simply discloses the encapsulation of an active substance in a liposome, protected with a gelatin shell, which may also be coated with a cellulosic polymer, and BAKER discloses lipidic vesicles comprising an active substance encapsulated in either the aqueous core or within the lipidic bilayer of said vesicles.

Thus, the combination fails to teach the modification by chemical species of the outer surface of an essentially hydrophilic matrix containing an active substance, wherein upon contact with microvilli during passage through the intestinal lumen, the species detach from the matrix such that the matrix becomes essentially hydrophilic in nature.

Therefore, withdrawal of the rejection is respectfully requested.

Conclusion

In view of the foregoing remarks, this application is in condition for allowance at the time of the next Official Action. Allowance and passage to issue on that basis is respectfully requested.

Should there be any matters that need to be resolved in the present application, the Examiner is respectfully requested to contact the undersigned at the telephone number listed below.

The Commissioner is hereby authorized in this, concurrent, and future submissions, to charge any deficiency or credit any overpayment to Deposit Account No. 25-0120 for any additional fees required under 37 C.F.R. § 1.16 or under 37 C.F.R. § 1.17.

Respectfully submitted,

YOUNG & THOMPSON

/Robert A. Madsen/

Robert A. Madsen, Reg. No. 58,543
209 Madison Street, Suite 500
Alexandria, VA 22314
Telephone (703) 521-2297
Telefax (703) 685-0573
(703) 979-4709

RAM/jr